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d) amplifying DNA fragments of the sample through the use of the adaptors. --

REMARKS

I. CLAIMS IN THE CASE

Claims 126 and 128 have been canceled without prejudice. Claims 105, 127 and 129 have been amended. Claims 136-152 have been added. Claims 105, 106, 112-115 and 123-152 are currently pending.

Claim 105 has been amended to introduce the concept of attaching an oligonucleotide adaptor to only one strand of the conditioned DNA fragment, as exemplified by canceled claim 128.

Additionally, new claims 136-152 have been added. These claims are directed to the subject matter of original claims 112-115, which were found allowable in the subject Official Action. Thus, claims 136-152 should be, on their face, in condition for allowance.

II. REINSTATEMENT OF CLAIMS 107-111 AND 116-122

In the subject Official Action, the Examiner inappropriately withdrew claims 107-11 and 116-122 under 37 C.F.R. §1.142(b) as drawn to non-elected inventions. However, 37 C.F.R. §1.142 is concerned with restriction requirements, not election of species. Election of species is dealt with under 37 C.F.R. §1.146, which does not provide for unilateral withdrawal of claims by the Examiner. The Examiner may also wish to review 37 C.F.R. §1.141, which permits applications to contain more than one patentably distinct species where a claim generic to those species is found, as well as MPEP §809.02(a), which contains no provisions permitting unilateral withdrawal of claims by examiners where, as here, there is a generic claim pending.

Applicants therefore hereby request reinstatement of claims 107-111 and 116-122 withdrawn by the Examiner pursuant to an election of species requirement. Reinstatement of the

claims is appropriate where, as here, a generic linking claim is allowable. For the reasons set forth below, current pending claim 105 is very clearly patentable over the art and constitutes a generic linking claim.

III. PRIORITY CLAIM/REQUEST FOR AMENDED FILING RECEIPT

In the subject Official Action, the Examiner observes that the present claims do not find support in an application inadvertently listed as a related application under 35 U.S.C. §120, Applicants apologize for this oversight and have made the appropriate amendments to the continuing application data. Applicants further request an amended filing receipt that reflects the corrected continuing application data.

IV. REJECTION OF CLAIMS UNDER 35 U.S.C. § 112, 2ND PARAGRAPH

The Action first rejects claims 123-125 as being indefinite in their suggestion that the 3' exonuclease "incorporates" a 3' hydroxyl. The Examiner suggests that it would be more appropriate for the claims to recite that the 3' exonuclease "produces" a 3' hydroxyl rather than incorporating one.

In response, Applicants agree that the wording may not have been entirely descriptive of the underlying mechanism, which involves revealing an existing 3'-OH instead of incorporating a new 3'OH, and thus have amended the claims to use the word "provide" a 3'-OH. Applicants appreciate the Examiner's suggestions.

V. REJECTION OF CLAIMS 105, 106, 123, 126 AND 127 AS ANTICIPATED

The Action next rejects claims 105, 106, 126 and 127 as anticipated by Legrain *et al.*, arguing that Legrain teaches a method of fragmenting by sonication and conditioning of 3' ends with Mung bean nuclease which, according to the Action, produces a 3' end with a 3' hydroxyl group.

Applicants point out that current main claim 105 is directed to the subject matter of previous claim 128, which concerned ligating an adaptor to the conditioned DNA fragment at only a single strand. This is achieved in the case of a double stranded adaptor through the use of an adaptor that has a blocked 3' or 5' terminus (see, *e.g.*, specification at Example 10, page 150, which includes a description of the use of a blocked 3'-termini adaptor).

In contrast, the reaction described by Legrain at column 30, beginning at line 40, would appear to result in the attachment of the adaptor by both strands rather than at a single strand as required by present claim 105 and dependents therefrom, and, in particular, does not appear to otherwise teach or suggest the attachment of an adaptor by only one strand, and does not appear to teach or suggest the attachment of an adaptor having a blocked terminus. If the Examiner is aware of any such teaching or suggestion from Legrain, the Examiner is requested to identify the teaching that is being relied upon in this regard.

VI. REJECTION OF CLAIMS 124, 125 AND 128-135 AS OBVIOUS

The Action next rejects claims 124, 125 and 128-135 as obvious over Legrain in combination with Willems, arguing that Willems teaches the additional features of treatment with exonuclease III, ligation to double stranded adaptors and amplification.

Applicants respond in the same manner as discussed above with respect to the rejection of claims 105, 106, 126 and 127. Although the Examiner included a rejection of claim 128 in this rejection, Applicants have been unable to find any teaching or suggestion in Willems regarding attaching an adaptor by only a single terminus as opposed to both termini. Thus, there is no *prima facie* basis for the rejection.

VII. NEW CLAIMS 136-152

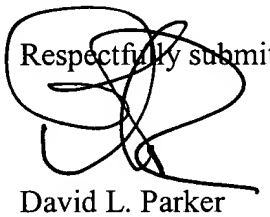
New claims 136-152 have been introduced and are directed to subject matter found allowable in the subject Official Action and thus should be in condition for allowance.

VIII. CONCLUSION

It is believed that the present response is a complete response to the outstanding official action, and that the present application is now in condition for allowance.

The Examiner is invited to contact the undersigned attorney at (512) 536-3055 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,



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Date: July 3, 2003

APPENDIX 1
AMENDMENTS TO SPECIFICATION

The paragraph beginning at page 2, line 3, is revised as follows:

-- The present application is a continuation of U.S. Patent Application Serial No. 09/151,236, filed September 10, 1998, now U.S. Patent 6,197,557, which was a continuation-in-part of co-pending U.S. Patent Application Serial No. 09/035,677, filed March 5, 1998,~~, which is a continuation-in-part of co-pending U.S. Patent Application Serial No. 08/811,804 filed March 5, 1997, t~~ The entire texts of the foregoing applications, ~~which~~, together with that of U.S. Patent Application Serial No. 08/811,804, are specifically incorporated herein by reference without disclaimer. The government owns rights in the present invention pursuant to grant number MCB 9514196 from the National Science Foundation. –

APPENDIX 2

CLAIM AMENDMENTS WITH MARKINGS

105. (Amended) A method for preparing a DNA molecule comprising the steps of:

a) obtaining a sample of DNA wherein the sample includes DNA fragments that do not include a 3' hydroxyl group; ~~and~~

b) conditioning DNA fragments of the sample to provide ~~that lack a 3' hydroxyl by incorporating~~ a 3' hydroxyl group thereon; and

c) attaching an oligonucleotide adaptor to only one strand of the conditioned DNA fragment.

~~126. The method of claim 105, further comprising attaching an oligonucleotide adaptor to the conditioned DNA fragments.~~

127. (Amended) The method of claim 105~~26~~, wherein the oligonucleotide adaptor is a double-stranded oligonucleotide adaptor.

~~128. The method of claim 127, wherein the double-stranded oligonucleotide adaptor is attached to the conditioned DNA by only one of its two strands.~~

129. (Amended) The method of claim 127~~8~~, wherein the double stranded adaptor is attached to the conditioned DNA by means of a 5' terminus of the adaptor.

New Claims 136-152:

--136. A method for preparing a DNA molecule comprising the steps of:

a) obtaining a sample of DNA wherein the sample includes DNA fragments that do not include a 3' hydroxyl group, wherein the DNA molecules have been fragmented by chemical means; and

b) conditioning DNA fragments of the sample to provide a 3' hydroxyl group thereon.

137. The method of claim 136, wherein the DNA molecules have been fragmented through a reaction that includes hydroxyl radicals.

138. The method of claim 137, wherein the DNA molecules have been fragmented through treatment with a Fenton reagent.

139. The method of claim 138, wherein the Fenton reagent comprises a metal ion chelating agent and a divalent metal ion.

140. The method of claim 136, wherein DNA fragments that lack a 3' hydroxyl are conditioned through the use of a 3' exonuclease.

141. The method of claim 140, wherein the 3' exonuclease is exonuclease III.

142. The method of claim 136, wherein the DNA fragments that lack a 3' hydroxyl are conditioned through the use of a DNA polymerase that possesses 3' to 5' exonuclease activity.

143. The method of claim 136, further comprising attaching an oligonucleotide adaptor to the conditioned DNA fragments.

144. The method of claim 143, wherein the oligonucleotide adaptor is a double-stranded oligonucleotide adaptor.

145. The method of claim 144, wherein the double-stranded oligonucleotide adaptor is attached to the conditioned DNA by only one of its two strands.

146. The method of claim 145, wherein the double stranded adaptor is attached to the conditioned DNA by means of a 5' terminus of the adaptor.

147. The method of claim 146, wherein the double-stranded oligonucleotide adaptor is blocked at at least one of its 3' termini.

148. The method of claim 147, wherein the double-stranded oligonucleotide adaptor is blocked at both of its 3' termini.

149. The method of claim 136, wherein the conditioned DNA fragments are amplified.

150. The method of claim 149, wherein DNA fragments are amplified through a PCR reaction.

151. The method of claim 150, wherein the DNA fragments are amplified through a PCR reaction through the use of double-stranded adaptors that have been attached to the conditioned DNA fragments.

152. The method of claim 136, further defined as comprising the steps of:

a) obtaining a sample of DNA wherein the sample includes DNA fragments that do not include a 3' hydroxyl group, wherein the sample has been subjected to fragmentation;

b) conditioning DNA fragments of the sample that lack a 3' hydroxyl by incorporating a 3' hydroxyl group thereon;

c) attaching adaptors to DNA fragments of the sample; and

d) amplifying DNA fragments of the sample through the use of the adaptors. --

PENDING CLAIMS FOLLOWING AMENDMENTS

105. A method for preparing a DNA molecule comprising the steps of:

a) obtaining a sample of DNA wherein the sample includes DNA fragments that do not include a 3' hydroxyl group;

b) conditioning DNA fragments of the sample to provide a 3' hydroxyl group thereon; and

c) attaching an oligonucleotide adaptor to only one strand of the conditioned DNA fragment.

106. The method of claim 105, wherein DNA molecules of the DNA sample have been fragmented.

107. The method of claim 106, wherein the DNA molecules have been fragmented by physical means.

108. The method of claim 107, wherein the DNA molecules have been fragmented by sonication.

109. The method of claim 107, wherein the DNA molecules have been fragmented by nebulization.

110. The method of claim 107, wherein the DNA molecules have been fragmented by hydrodynamic shear.

111. The method of claim 107, wherein the DNA molecules have been fragmented by freezing and thawing.

112. The method of claim 106, wherein the DNA molecules have been fragmented by chemical means.

113. The method of claim 107, wherein the DNA molecules have been fragmented through a reaction that includes hydroxyl radicals.

114. The method of claim 113, wherein the DNA molecules have been fragmented through treatment with a Fenton reagent.

115. The method of claim 114, wherein the Fenton reagent comprises a metal ion chelating agent and a divalent metal ion.

116. The method of claim 106, wherein the DNA molecules have been fragmented by enzymatic means.

117. The method of claim 116, wherein the DNA molecules have been fragmented using an endonuclease.

118. The method of claim 116, wherein the DNA molecules have been fragmented through the use of a restriction endonuclease.

119. The method of claim 118, wherein the DNA molecules have been fragmented through the use of a restriction endonuclease having a two base recognition sequence.

120. The method of claim 118, wherein the DNA molecules have been fragmented through the use of a restriction endonuclease having a four base recognition sequence.

121. The method of claim 118, wherein the restriction endonuclease has introduced random double strand breaks into DNA molecules.

122. The method of claim 117, wherein the endonuclease introduced a blunt end.

123. The method of claim 105, wherein DNA fragments that lack a 3' hydroxyl are conditioned through the use of a 3' exonuclease.

124. The method of claim 123, wherein the 3' exonuclease is exonuclease III.

125. The method of claim 105, wherein the DNA fragments that lack a 3' hydroxyl are conditioned through the use of a DNA polymerase that possesses 3' to 5' exonuclease activity.

127. The method of claim 105, wherein the oligonucleotide adaptor is a double-stranded oligonucleotide adaptor.

129. The method of claim 127, wherein the double stranded adaptor is attached to the conditioned DNA by means of a 5' terminus of the adaptor.

130. The method of claim 129, wherein the double-stranded oligonucleotide adaptor is blocked at at least one of its 3' termini.

131. The method of claim 130, wherein the double-stranded oligonucleotide adaptor is blocked at both of its 3' termini.

132. The method of claim 105, wherein the conditioned DNA fragments are amplified.

133. The method of claim 132, wherein DNA fragments are amplified through a PCR reaction.

134. The method of claim 133, wherein the DNA fragments are amplified through a PCR reaction through the use of double-stranded adaptors that have been attached to the conditioned DNA fragments.

135. The method of claim 105, further defined as comprising the steps of:

a) obtaining a sample of DNA wherein the sample includes DNA fragments that do not include a 3' hydroxyl group, wherein the sample has been subjected to fragmentation;

b) conditioning DNA fragments of the sample that lack a 3' hydroxyl by incorporating a 3' hydroxyl group thereon;

c) attaching adaptors to DNA fragments of the sample; and

d) amplifying DNA fragments of the sample through the use of the adaptors.

136. A method for preparing a DNA molecule comprising the steps of:

a) obtaining a sample of DNA wherein the sample includes DNA fragments that do not include a 3' hydroxyl group, wherein the DNA molecules have been fragmented by chemical means; and

b) conditioning DNA fragments of the sample to provide a 3' hydroxyl group thereon.

137. The method of claim 136, wherein the DNA molecules have been fragmented through a reaction that includes hydroxyl radicals.

138. The method of claim 137, wherein the DNA molecules have been fragmented through treatment with a Fenton reagent.

139. The method of claim 138, wherein the Fenton reagent comprises a metal ion chelating agent and a divalent metal ion.

140. The method of claim 136, wherein DNA fragments that lack a 3' hydroxyl are conditioned through the use of a 3' exonuclease.

141. The method of claim 140, wherein the 3' exonuclease is exonuclease III.

142. The method of claim 136, wherein the DNA fragments that lack a 3' hydroxyl are conditioned through the use of a DNA polymerase that possesses 3' to 5' exonuclease activity.

143. The method of claim 136, further comprising attaching an oligonucleotide adaptor to the conditioned DNA fragments.

144. The method of claim 143, wherein the oligonucleotide adaptor is a double-stranded oligonucleotide adaptor.

145. The method of claim 144, wherein the double-stranded oligonucleotide adaptor is attached to the conditioned DNA by only one of its two strands.

146. The method of claim 145, wherein the double stranded adaptor is attached to the conditioned DNA by means of a 5' terminus of the adaptor.

147. The method of claim 146, wherein the double-stranded oligonucleotide adaptor is blocked at at least one of its 3' termini.

148. The method of claim 147, wherein the double-stranded oligonucleotide adaptor is blocked at both of its 3' termini.

149. The method of claim 136, wherein the conditioned DNA fragments are amplified.

150. The method of claim 149, wherein DNA fragments are amplified through a PCR reaction.

151. The method of claim 150, wherein the DNA fragments are amplified through a PCR reaction through the use of double-stranded adaptors that have been attached to the conditioned DNA fragments.

152. The method of claim 136, further defined as comprising the steps of:

a) obtaining a sample of DNA wherein the sample includes DNA fragments that do not include a 3' hydroxyl group, wherein the sample has been subjected to fragmentation;

b) conditioning DNA fragments of the sample that lack a 3' hydroxyl by incorporating a 3' hydroxyl group thereon;

c) attaching adaptors to DNA fragments of the sample; and

d) amplifying DNA fragments of the sample through the use of the adaptors.